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September 26, 2003

Mr. Jon Epperson
U.S. Patent Office
7th Floor Receptions Area
1911 South Clark Place
Crystal Mall One
Arlington, VA 22202

Re: Patent Application Serial Number 09/804,893
Response to Office Communication of 3/28/2003

ATTN: Jon Epperson

Dear Mr. Epperson:

This is a response to your communication dated March 28, 2003. We would like to make the following observations and comments:

Response to Restriction and/or Election of Species

We respectfully request that the examiner reconsider his conclusion that "the methods are distinct because they use different reaction steps,.." (page 4 #11). We had previously stated that that different reaction steps are not required to affect the claimed method, which is contacting a biomolecule with the reactive dye as generically, claimed. The reaction with the biomolecule is through the phosphoramidite to a hydroxyl group on the biomolecule (B), or via the hydroxyl group and an amine terminated linker (L). There is no difference in this reaction step for any of the structurally different D (and L and B). Therefore we respectfully suggest that only one method is claimed, and would not require separate and burdensome searches.

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We request that the examiner reconsider the exclusion of Claim 23, as " a non-elected species" It is in Claim 23 that we claim the species, which are biomolecules as defined by B.

Claims Rejections

20. A

We would like to clarify the phrase " wherein the linear atoms in L...optionally can be included in a ring", as you have requested. The linear atoms optionally can be in the form of a ring, such that six linear atoms would form a benzene ring, for example. Our intention is that the number of linear atoms can be linear, or in the form of a ring. The suggested wording would change to "wherein the linear atoms in L...optionally would form or comprise a ring."

20. B. We respond to your request for a clarification of the phrase "provided that D is not unsubstituted perylenyl" by suggesting that this phrase be deleted. We trust that this clarification will meet with your approval.

Claims Rejections – 35 U.S.C. 102

Anticipation by Bevers, et. al.

The Bevers et. al. publications describe research relating to hairpin and duplex nucleic acid structures. They report that such duplex and triplex structures can be stabilized by tethering together two of the nucleic acid strands by means of a chemical linker. In particular, the publications point out the stabilizing effect of linkers containing molecules such as perylene diimide. This strong stabilizing effect is attributed to stacking interactions. "Detection" of the biomolecule by melting studies using absorption measurements does not anticipate our invention. The publications provide no indication that visual-to-the naked eye observation of color was considered in any way useful or significant.

Bevers et.al publications relate to the stabilization of nucleic acid duplex and triplex structures by crosslinking two nucleic acid strands with an aromatic linker. They do not suggest any purpose for these moieties other than their use as crosslinkers. Our invention is limited to compounds wherein each dye molecule forms a single linkage

to a biomolecule, thereby excluding the crosslinked oligos described in the Bevers et. Al. publications.

We respectfully request the examiner to reconsider anticipation by the Bevers publications.

Anticipation by Suzuki, et.al.

Suzuki et.al. does not cite perylenes or perylenyl moieties in his invention. Also, the Suzuki invention is for fluorescent compounds, whereas our invention is for biolabels which are visually detected with the naked eye.

Anticipation by Balakin, et. Al.

Balakin et al is directed to the use of pyrene and perylene conjugates as fluorescent labels, and makes no mention of the labels, which can be attached to oligos, which render them, visual to the naked eye. Balakin refers to perylene as a fluorescent molecule.

We do not make claims regarding the fluorescent properties of our moieties, and Balakin makes no claims that his invention has visual-to-the-naked eye properties.

Anticipation by Kool et al

Kool et. Al. does not anticipate our invention since all of his compounds are chosen for their fluorescent properties, and the Kool et. Al. invention rests upon fluorescent compounds connected with simple sugars. Our invention relates to the visual properties of our compounds, and to the use with oligonucleotides such as DNA, RNA, proteins and antibodies. Likewise Kool disclosed a phosphoramidite which is attached to a simple sugar, and the goal is its fluorescent properties. Our invention relates to a connection with a biomolecule, for its visual properties. In addition, the reaction of our biolabel –linker with a biomolecule such as DNA and RNA is different that the reaction of Kool's fluorescent labels with simple sugars, due to steric hinderage, solution dynamics and kinetic issues. Also, Kool incorporates the phosphoramidite-sugar-label with a synthesizer, and our invention directly combines a phosphoramidite-label with the synthesis of an olignucleotide in a synthesizer. Therefore, we do not believe that Kool anticipates our invention.

Enclosed herewith is a check in the amount of $ 985.00 in payment of the three-month extension fees, as a small business entity. Please grant any extensions of time required to enter this response.

Thank you for your consideration.

Very truly yours,

George R. Berbeco
President

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